critically dependent on HIF1α but not hypoxia-inducible factor-2 alpha, but critically dependent on HIF2α in the renal carcinoma cells. Sowter *et al.*, 2003, *Cancer Res., 63*, 6130-6134.

Please replace paragraph [0050] with the following:

[0050] The present invention provides compositions and methods for modulating HIF1α and HIF2α expression. In particular antisense compositions for modulating HIF1α and/or HIF2α expression are believed to be useful in treatment of abnormal proliferative conditions associated with HIF1α and/or HIF2α. Examples of abnormal proliferative conditions are hyperproliferative disorders such as cancers, tumors, hyperplasias, pulmonary fibrosis, angiogenesis, psoriasis, atherosclerosis and smooth muscle cell proliferation in the blood vessels, such as stenosis or restenosis following ~~antioplasty~~ angioplasty. It is presently believed that inhibition of both HIF1α and HIF2α may be a particularly useful approach to treatment of such disorders.

Please replace paragraph [0089] with the following:

[0089] Such double stranded oligonucleotide moieties have been shown in the art to modulate target expression and regulate translation as well as RNA ~~processing~~ processing via an antisense mechanism. Moreover, the double-stranded moieties may be subject to chemical modifications (Fire *et al.*, *Nature*, **1998**, *391*, 806-811; Timmons and Fire, *Nature* **1998**, *395*, 854; Timmons *et al.*, *Gene*, **2001**, *263*, 103-112; Tabara *et al.*, *Science*, **1998**, 282, 430-431; Montgomery *et al.*, *Proc. Natl. Acad. Sci. USA*, **1998**, *95*, 15502-15507; Tuschl *et al.*, *Genes Dev.*, **1999**, *13*, 3191-3197; Elbashir *et al.*, *Nature*, **2001**, *411*, 494-498; Elbashir *et al.*, *Genes Dev.* **2001**, *15*, 188-200). For example, such double-stranded moieties have been shown to inhibit the target by the classical hybridization of antisense strand of the duplex to the target, thereby triggering enzymatic degradation of the target (Tijsterman *et al.*, *Science*, **2002**, *295*, 694-697).

Please replace paragraph [0168] with the following: MW 1-2-07

[0168] RNA strands of the duplex can be synthesized by methods disclosed herein or purchased from Dharmacon Research Inc., (Lafayette, CO). Once synthesized, the complementary strands are annealed. The single strands are ~~aliquoted~~ aliquotted and diluted to a concentration of 50 uM. Once diluted, 30 uL of each strand is combined with 15uL of a 5X solution of annealing buffer. The final concentration of said buffer is 100 mM potassium acetate, 30 mM HEPES-KOH pH 7.4, and 2mM magnesium acetate. The final volume is 75 uL. This

PAGE 7/23 * RCVD AT 9/27/2006 12:14:09 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-6/6 * DNIS:2738300 * CSID:7606033820 * DURATION (mm-ss):03-44

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solution is incubated for 1 minute at 90°C and then centrifuged for 15 seconds. The tube is allowed to sit for 1 hour at 37°C at which time the dsRNA duplexes are used in experimentation. The final concentration of the dsRNA duplex is 20 uM. This solution can be stored frozen (-20°C) and freeze-thawed up to 5 times.

Please replace paragraph [0181] with the following: 180

MW 1-2-07

[0181] The mouse brain endothelial cell line b.END was obtained from Dr. Werner Risau at the Max Plank ~~Instititute~~ Institute (Bad Nauheim, Germany). b.END cells were routinely cultured in DMEM, high glucose (Gibco/Life Technologies, Gaithersburg, MD) supplemented with 10% fetal calf serum (Gibco/Life Technologies, Gaithersburg, MD). Cells were routinely passaged by trypsinization and dilution when they reached 90% confluence. Cells were seeded into 96-well plates (Falcon-Primaria #3872) at a density of 3000 cells/well for use in RT-PCR analysis.

Please replace paragraph [0191] with the following: 190

MW 1-2-07

[0191] Analysis of the ~~genecotype~~ genotype of the cell (measurement of the expression of one or more of the genes of the cell) after treatment is also used as an indicator of the efficacy or potency of the HIF1α and/or HIF2α inhibitors. Hallmark genes, or those genes suspected to be associated with a specific disease state, condition, or phenotype, are measured in both treated and untreated cells.

PAGE 8/23 * RCVD AT 9/27/2006 12:14:09 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-5/6 * DNIS:2738300 * CSID:7606033820 * DURATION (mm-ss):03-44

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Amendments to the Specification:

Please replace paragraph no [0~~166~~] 165 with the following rewritten paragraph: MW 1-2-07

-- [0~~166~~] 165 For example, a duplex comprising an antisense strand having the sequence CGAGAGGCGGACGGGACCG (SEQ ID NO: 455) and having a two-nucleobase overhang of deoxythymidine(dT) would have the following structure:

```
cgagaggcggacgggaccgTT    Antisense Strand (SEQ
                                ID NO: 456)
                  ||||||||||||||||||
TTgctctccgcctgccctggc     Complement (SEQ ID NO:
                                457)--
```

Please replace paragraph no [0~~167~~] 166 with the following rewritten paragraph: MW 1-2-07

-- [0~~167~~] 166 As another example, a duplex comprising an antisense strand having the sequence CGAGAGGCGGACGGGACCG (SEQ ID NO: 455) and having no overhangs would have the following structure:

```
cgagaggcggacgggaccg      Antisense Strand(SEQ
                                ID NO: 455)
                  ||||||||||||||||||
gctctccgcctgccctggc       Complement (SEQ ID NO:
                                458)--
```


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